

invention unless they are *absolutely* identical. Such a holding would also mean that Examiners could not issue prior art rejections of DNA claims unless the prior art DNA is *absolutely* identical to the claimed DNA.

AMENDMENT

Please amend the above-identified application as follows:

IN THE CLAIMS

Please delete claims 83 and 91-97 without prejudice to or disclaimer of the subject matter contained therein.

REMARKS

Entry of the foregoing, and further and favorable reconsideration of the subject application and Applicants' second renewed request for interference are respectfully requested. The status as of the date of this amendment of all patent claims, and of all added claims, is attached hereto as Appendix A in accordance with 37 CFR 1.124(b)(2)(ii). A copy of the pending claims is attached as Appendix Q.

Applicants gratefully acknowledge the courtesy shown to their representatives by Examiner Moore. During a telephone conference on April 25, 2001, the Examiner indicated that while pending claims 1-82 and 84-90 are allowable, claims 83 and 91-97 would be subject to a rejection under 35 USC §135(b) over one or more of U.S. Patents 4,968,626, 5,302,529 and 5,073,609 to Foster. Applicants do not agree that such a rejection is appropriate. Nevertheless, in an effort to expedite prosecution, by the present amendment claims 83 and 91-97 have been deleted without prejudice or disclaimer.

Applicants further gratefully acknowledge the courtesy shown to their representatives in the personal interview held on April 26, 2001 with Special Programs Examiner Caputa,

Supervisory Primary Examiner Achutamurthy, and Examiner Moore. In the personal interview, Applicants presented a new proposed Count, and submitted other exhibits and made arguments in support of the position that an interference is appropriate between the Bang application and U.S. Patents 4,968,626, 5,302,529 and 5,073,609 to Foster. The claims of the Foster patents are attached hereto as Appendix C.

New Proposed Count

The new proposed Count is attached hereto as Appendix B. The new proposed Count contains, in the alternative, claim 2 of the Bang application ("Bang claim 2"), and claims 3 and 4 of the Foster '529 Patent. Since all three of these claims are directed to a plasmid comprising nearly identical cDNA sequences encoding exactly the same human protein C, there can be no question but that the requirement of two-way obviousness is satisfied. Indeed, the corresponding sequences of Bang claim 2 and Foster '529 claims 3 and 4 encode identical amino acid sequences.

There are only two nucleotide differences between the cDNA sequences of Bang claim 2 and Foster '529 claims 3 and 4. Those nucleotide differences appear in the third position of codons 99 and 214, and have no effect upon the resulting amino acid. The DNA sequence of Bang claim 2 and that of Foster '529 claims 3 and 4 encode SER at position 99 and ASP at position 214.

With knowledge of the codons appearing at positions 99 and 214 of Bang claim 2, a person skilled in the art could readily use a codon table to determine the corresponding codons of Foster '529 claim 3 and 4. Conversely, with knowledge of the codons appearing at positions 99 and 214 of Foster '529 claims 3 and 4, that person could use a codon table to determine the codons of Bang claim 2. All remaining nucleotides of the Bang and Foster protein C sequences are identical.

The new proposed Count employs the sequences set forth in the respective application and patents. However, as explained in detail below, it is very likely that the actual Foster sequence is identical to the corresponding Bang sequence. Indeed, the sequence deposited by Foster in GenBank is identical to the corresponding sequence in claim 1 of the Bang application. As such, the differences between the Foster cDNA sequence, and the sequence of the Bang application, are probably due to sequencing errors on the part of Foster.

The Bang and Foster Sequences are Virtually Identical

Bang claim 2 is directed to a plasmid comprising the four alternative human protein C cDNA molecules of Bang claim 1, and Foster '529 claims 3 and 4 are directed to two of those four alternatives. Bang claim 1 includes a zymogen sequence, and definitions of a *pre* and a *pro* sequence ("R1" and "R"). The four alternatives are (1) the zymogen alone, (2) the zymogen plus a *pro* sequence, (3) the zymogen plus a *prepro* sequence, and (4) the zymogen plus a truncated *prepro* sequence. These four alternatives, and how the Foster claim 3 and 4 sequences correspond to them, are explained in detail in Appendix D.

All three claims that make up the proposed Count are species claims, directed to specific cDNA sequences which encode identical amino acid sequences. As can be seen from Appendix D, Bang claim 2 is directed to a plasmid comprising four alternative human protein C cDNA molecules :

- 1) cDNA encoding human protein C zymogen;
- 2) cDNA encoding human protein C zymogen and additional cDNA encoding a short (9 or 10 amino acid) *pro*- sequence;
- 3) cDNA encoding human protein C zymogen, the 9 or 10 amino acid *pro* sequence, and a short (32 or 33 amino acid) *pre*- sequence; and
- 4) cDNA encoding human protein C zymogen, and cDNA encoding a truncated *prepro*- sequence.

The second part of the new proposed Count represents claim 3 of the Foster '529 patent. This claim is directed to a plasmid or bacteriophage transfer vector comprising cDNA encoding human protein C zymogen, alternative (1) above. Foster '529 claim 3 defines a cDNA sequence which:

- is identical to Bang claim 2 in the number of nucleotides;
- encodes exactly the same amino acids as Bang claim 2; and
- is nearly identical to alternative (1) of the four cDNA sequences of Bang claim 2 set forth above.

The third part of the new proposed Count represents claim 4 of the Foster '529 patent. This claim is directed to a plasmid or bacteriophage transfer vector encoding human *prepro* protein C, alternative (3) above. Foster '529 claim 4 likewise defines a cDNA sequence which:

- is identical to Bang claim 2 in the number of nucleotides;
- encodes exactly the same amino acids as Bang claim 2; and
- is nearly identical to the alternative (3) of the four cDNA sequences of Bang claim 2 set forth above.

The Differences Between the Bang and Foster Sequences are Probably Foster Mistakes

As the Patent Office has recently recognized, it is well known that sequencing errors are a common problem in molecular biology¹. Evidence supporting the conclusion that the differences between the Bang and Foster sequences are due to sequencing errors by Foster may be found within the Foster patents themselves: the protein C DNA sequence shown in Figure 2 of Foster contains only one of the base differences: that at position 99. Further evidence may be found in publications of Foster. Specifically, Foster published articles in the *Proceedings of the National Academy of Sciences* that showed DNA sequences matching both

¹"Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, 'Written Description' Requirement." 66 Fed. Reg. 1099, 1108, n. 19

Patent Figure 3 (two base differences) and Figure 2 (one base difference).² Later, Foster made a deposit of their protein C DNA sequence in GenBank; this deposited sequence is *identical* to the sequence in the Bang application. This information strongly suggests that the sequence differences between the Bang sequence, and Foster Figure 3, are due to sequencing errors on the part of Foster.

The nucleotide differences between the Bang and Foster sequences are silent – *i.e.*, the differences in the last nucleotide of codon 99 and/or the last nucleotide of codon 214 do not affect the identity of the amino acids encoded by those two codons. Moreover, there is at most a two-nucleotide difference between the Bang and the Foster sequences out of 1,257 nucleotides (99.84% homology). If the leader sequence of forty-two (42) additional codons is taken into consideration, there is at most a two-nucleotide difference out of 1,383 nucleotides (99.86% homology).

The chart below summarizes information contained in various documents where the Bang and Foster sequences are disclosed.

Description	Tab	Last Nucleotide of Codon 99	Last Nucleotide of Codon 214
Bang Reissue Application No. 09/185,663	E	G	T
Bang GenBank Sequence X02750	F	G	T
Foster GenBank Sequence nm_000312	G	G	T
Foster '626 Patent (Figure 2*/Figure 3**)	H	T/T	T/C
Foster '609 Patent (Figure 2*/Figure 3**)	I	T/T	T/C
Foster '529 Patent (Figure 2*/Figure 3**)	J	T/T	T/C
Foster PNAS '84	K	T	C
Foster PNAS '85	L	T	T

* Figure 2 is the complete genomic sequence for human protein C.

**Figure 3 is the amino acid and DNA sequence for a cDNA coding for human protein C.

²Figures 2 and 3 are identical in the three Foster patents.

The relevant documents are also attached hereto. Applicants submit that this evidence, when viewed as a whole, clearly supports the conclusion that the two nucleotide differences in the Foster sequence are due to sequencing errors, and not to true differences in cDNA sequence.

At this time, review of Applicants' renewed request for interference is appropriate.

Applicants' renewed request for interference is as follows:

REQUEST FOR INTERFERENCE

I. IDENTIFICATION OF THE PATENTS

Applicants request that an interference be declared between the Bang application and U.S. Patent Nos. 4,968,626, 5,073,609, and 5,302,529 to Foster ("the Foster '626 Patent," "the Foster '609 Patent," and "the Foster '529 Patent", respectively). For the reasons set forth below, it is apparent that all three Foster Patents should be involved in the requested interference.

All three Foster Patents originate from a common original application for patent and share a common specification. The '609 and '529 Patents issued as voluntary divisional applications in which terminal disclaimers were filed to obtain their issuance. For both Patents, double patenting rejections were made that were not traversed. Hence, the claims of the '626 Patent, the '609 Patent, and the '529 Patent can be regarded as patentably indistinct from each other – they share a common specification, they are bundled together via terminal disclaimers, and they exist separately only because of prosecution decisions by Foster to divide the claims apart. As the CCPA noted in *In re Braithwaite*, 154 USPQ 29, 34 (CCPA 1967), "[w]hen a terminal disclaimer causes two patents to expire together a situation is created which is tantamount for all practical purposes to having all the claims in one patent." Accordingly, in proposing a count and determining which claims should correspond to the proposed Count, the three Foster Patents have been treated as a single patent.

II. PRESENTATION OF PROPOSED COUNT

Attached Appendix B sets forth a proposed Count. The proposed Count is an alternative Count prepared after consideration of the subject matter claimed by the respective parties. As required by 37 CFR 1.601(f) as recently amended, the proposed Count "defines the interfering subject matter between ... one or more applications and one or more patents."

The interfering subject matter between Bang and Foster relates to the cDNA encoding human protein C. The proposed Count is directed to claim 2 of the Bang application and claims 3 and 4 of the Foster '529 Patent, in the alternative. All three claims are directed to plasmids comprising cDNA encoding human protein C. Claim 2 of the Bang application is directed to a plasmid comprising cDNA encoding the human protein C zymogen, with or without the addition of the relevant *pre* or *prepro* cDNA sequences. Claim 3 of the Foster '529 Patent claims a plasmid comprising cDNA encoding the human protein C zymogen. Claim 4 of the Foster '529 Patent claims a plasmid comprising cDNA encoding the human protein C zymogen, and the short *prepro* sequence.

As described *supra*, the three Foster Patents identified in this Request are effectively a single patent. Accordingly, only a single representative claim from the Foster Patents is required for the Count. However, because Claim 2 of the Bang application encompasses four different DNA molecules, Claims 3 and 4 of the Foster '529 Patent are both believed to be appropriate claims for the alternative Count because each claim is directed to a DNA molecule corresponding to a DNA molecule of Bang Claim 2.

Neither of the two claims of the Foster '609 Patent is an appropriate claim for the Count because these claims are directed to fragments of human protein C DNA (*i.e.*, DNA compounds consisting of the DNA that encodes only a part of the full DNA sequence needed to encode the complete protein). Under *Amgen v. Chugai*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), neither claimed fragment represents a complete conception of the protein C cDNA. Hence, the fragment claims are not appropriate for determining priority of invention for the interfering

subject matter (*i.e.*, the complete cDNA encoding human protein C), and thus are not appropriate for use in an interference count.

None of claims 1-3 of the Foster '626 Patent is an appropriate claim for the Foster portion of the proposed Count. Claim 1 of the Foster '626 Patent is a generic claim directed to any human DNA sequence encoding any protein having the activity of human protein C. This generic claim would not render obvious the specific cDNA sequence contained in the plasmid of Bang claim 2. Claim 2 of the Foster '626 Patent is directed to a DNA sequence comprising human protein C genomic DNA, rather than a cDNA sequence coding for human protein C. Claim 3 of the Foster '626 patent does not refer to the specific cDNA sequence of Figure 3.

In view of the above, only claims 3 and 4 of the Foster '529 Patent represent appropriate claims to serve as Foster's portion of the Count.

III. IDENTIFICATION OF CLAIMS OF THE FOSTER PATENTS WHICH CORRESPOND TO THE PROPOSED COUNT

Claims 1-3 of the Foster '626 Patent, claims 1-2 of the Foster '609 Patent, and claims 1-4 of the Foster '529 Patent, *i.e.*, all of the Foster claims, should be designated as corresponding to the proposed Count.

FOSTER '626 PATENT

Claims 1 and 3

As noted above, claim 1 of the Foster '626 Patent is a generic claim that encompasses any human DNA sequence encoding a protein with the activity of human protein C. Because the cDNA contained in the plasmid of the Count encodes human protein C, which indisputably is a protein with the activity of human protein C, that cDNA would anticipate claim 1 of the Foster '626 patent if it were prior art. The claims of the Count are directed to plasmids; however, Applicants maintain that it would have been obvious, at the time the present applications were filed, to remove the protein C cDNA from a plasmid containing such cDNA, with a reasonable

expectation of success, and without the need for undue experimentation. Claim 1 of the '626 Patent thus corresponds to the proposed Count.

Claim 3 of the Foster '626 Patent recites a bacterial plasmid or bacteriophage transfer vector comprising a cDNA sequence comprising the human protein C gene cDNA sequence. Such a cDNA sequence appears at Figure 3 of the '626 Patent, and Figure 3 of the Foster '529 Patent. Claims 3 and 4 of the '529 patent, which are part of the proposed Count, would anticipate claim 3 of the '626 Patent if they were prior art. The Count thus defines the same patentable invention as claim 3 of the Foster '626 Patent. Because of the use of the word "or," correspondence to at least one part of the proposed Count is sufficient.

Claim 2

Claim 2 of the Foster '626 Patent defines an "isolated DNA sequence comprising the sequence of FIG. 2, from bp 1 to bp 8972, which sequence codes for human protein C." Figure 2 of the Foster '626 Patent purports to describe the complete genomic DNA sequence for human protein C. As noted above, the claims of the Count are directed to plasmids *comprising* human protein C cDNA. The genomic sequence represents a DNA that includes the cDNA sequence, and contains additional DNA sequence. As such, claim 2 is rendered obvious by, and should also be designated as corresponding to the proposed Count.

FOSTER '609 PATENT

Claims 1 and 2

Claim 1 of the Foster '609 Patent, directed to the DNA sequence encoding the heavy chain of human protein C, and claim 2 of the Foster '609 Patent, directed to a DNA sequence encoding human protein C from amino acid 64 to amino acid 419 (*i.e.*, a fragment of the human protein C cDNA sequence), correspond to at least one part of the proposed Count. During prosecution of the application which became the Foster '609 Patent, the Examiner made an

obviousness-type double patenting rejection of these two claims over the claims of the Foster '626 Patent, because "it would be obvious to select and isolate fragments of the cDNA and genomic clone disclosed in said patent." See, paragraph bridging pages 2-3 of the Official Action dated December 27, 1990, attached as Appendix M. This rejection was not disputed by Foster, but instead was acquiesced to by filing a terminal disclaimer. See, page 2 of Foster's Response dated April 29, 1991, attached as Appendix N. Foster thus admitted that claims 1 and 2 of the '609 Patent are obvious in view of claims directed to Foster's full-length human protein C cDNA sequence. Claims obvious from the Count are directed to the same patentable invention as the Count, and thus must correspond to the Count. 37 CFR 1.601(n). These claims should, therefore, be so designated.

FOSTER '529 PATENT

Claims 1-4

Claims 3 and 4 of the Foster '529 Patent are part of the suggested Count. Claims 1 and 2 of the '529 Patent are directed to plasmids encoding the amino acid sequence of human protein C, as shown in Figure 3. Because of the redundancy of the genetic code, these claims are generic claims that encompass the specific cDNA sequences contained in the plasmids of the Count. The plasmids of claims 3 and 4 of the '529 patent would anticipate claims 1 and 2, if they were prior art. Therefore, claims 1 and 2 of the Foster '529 Patent are directed to the same invention as the proposed Count and correspond to the proposed Count.

IV. CLAIMS OF THE BANG REISSUE APPLICATION WHICH CORRESPOND TO THE PROPOSED COUNT

All pending claims in the Bang reissue application should be designated as corresponding to the proposed Count. The only difference between the present Request and the initial Request filed on August 9, 1999, is that Bang claims 81 and 82 are requested to be

designated as corresponding to the proposed Count for the same reasons that claims 1 and 2 of the Foster '609 Patent should be designated as corresponding to the Count.

V. APPLICATION OF TERMS OF APPLICATION CLAIMS

No new claims are being added to the Bang reissue application by this Request. A showing of the patentability of newly added claims thus is not required.

VI. EXPLANATION OF HOW THE REQUIREMENT OF 35 U.S.C. §135(b) IS MET

According to 35 USC §135(b), "[a] claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted."

In the instant case, it is clear that the requirement of §135(b) is met. Bang Patent claims 1-82 all issued long before any of the Foster Patent claims. Claims 1-82 of the Bang Patent issued in U.S. Patent No. 4,775,624 on October 4, 1988, *i.e.*, prior to the issuance of any of the Foster Patents. The Foster '626 Patent issued November 6, 1990, the Foster '609 Patent issued December 17, 1991, and the Foster '529 Patent issued April 12, 1994. Moreover, at the very least, Bang claims 1 and 2 as issued were originally presented as claims 1 and 2 in Application Serial No. 699,967, filed on February 8, 1985. Claims 1-82 of the Bang reissue application were thus present in the Bang Patent and as recited therein are "the same as, or for the same or substantially the same subject matter as, a claim of" the issued Foster Patents, and were present prior to one year from the dates on which the Foster '626 Patent, the Foster '609 Patent, and the Foster '529 Patent issued.

Further, during prosecution of the Foster '626 Patent, the pending Foster claims were rejected under 35 U.S.C. §102(e) and §103 over the Bang '624 Patent, which is being reissued by the Bang application. See, pages 4-5 of the Official Action dated June 2, 1989, in the

prosecution of the application which matured into the Foster '626 Patent, attached as Appendix O. The cloning and expression methods and compositions of Bang were said by the Examiner to anticipate the Foster claims. Since Foster was attempting to claim the same invention as already issued in the Bang Patent, the only way Foster should have been allowed to respond to the rejection would have been to file appropriate declarations pursuant to 37 C.F.R. §1.608(b) to provoke an interference.

"When the reference in question is a noncommonly owned patent claiming the same invention as applicant and its issue date is less than 1 year prior to the filing date of the application being examined, applicant's remedy, if any, must be by way of 37 CFR 1.608 instead of 37 CFR 1.131." MPEP §715.05. Nevertheless, the Examiner improperly withdrew the rejection over the Bang Patent in response to a Declaration by Foster under 37 CFR 1.131. Had Foster's improper §131 Declaration been refused, as it should have been, and Foster been forced to file one or more §1.608(b) Declarations, then the interference would have occurred prior to issuance of any of the Foster patents. This alone should be enough to satisfy §135(b).

VII. EXPLANATION OF WHY AN INTERFERENCE SHOULD BE DECLARED

As stated in 37 C.F.R. §1.601(i), "[a]n *interference* is a proceeding instituted in the Patent and Trademark Office before the Board to determine any question of patentability and priority of invention between two or more parties claiming the same patentable invention" [emphasis in original]. According to 37 C.F.R. §1.601(n), "[i]nvention A is the *same patentable invention* as an invention 'B' when invention 'A' is the same as (35 U.S.C. §102) or is obvious (35 U.S.C. §103) in view of invention 'B' assuming invention 'B' is prior art with respect to invention 'A'" [emphasis in original].

Claims 1-82 and 84-90 of the Bang application define the same patentable invention as claims 1-3 of the Foster '626 Patent, claims 1-2 of the Foster '609 Patent, and claims 1-4 of the Foster '529 Patent. All of the claims of these three Foster Patents, and all of the claims of the

Bang application, are directed to embodiments which recite a sequence encoding human protein C polypeptide, or embodiments which are anticipated by or obvious in view of such a sequence. By comparing the sequences disclosed in the Bang application to those in the Foster '626 Patent, the Foster '609 Patent and the Foster '529 Patent, it can be seen that the sequences are substantially the same.

The prosecution histories of the Foster '626 Patent, Foster '609 Patent, and the Foster '529 Patent also show that these three patents are claiming the same invention as Bang in the instant application. As discussed above, to obtain allowance, the Foster '529 Patent and the Foster '609 Patent were terminally disclaimed over the Foster '626 Patent to overcome obviousness-type double patenting rejections. See, paragraph bridging pages 2-3 of the Official Action dated December 27, 1990, attached as Appendix P. As also discussed above, during prosecution of the Foster '626 Patent, the pending Foster claims were rejected under 35 U.S.C. §102(e) and §103 over the Bang '624 Patent, which is being reissued by the instant application. See, pages 4-5 of the Official Action dated June 2, 1989, attached as Appendix O.

Because the claims of the Bang application and the Foster Patents all define the same patentable invention, an interference should be declared between claims 1-82 and 84-90 of the Bang application, claims 1-3 of the Foster '626 Patent, claims 1-2 of the Foster '609 Patent, and claims 1-4 of the Foster '529 Patent.

VIII. CONCLUSION

Applicants respectfully request that an interference be declared employing the proposed Count set forth on attached Appendix B with claims 1-82 and 84-90 of the Bang application, claims 1-3 of the Foster '626 Patent, claims 1-2 of the Foster '609 Patent, and claims 1-4 of the Foster '529 Patent designated as corresponding to the Count.

In the event that there are any questions relating to this paper, Applicants respectfully urge the Examiner to telephone the undersigned so that prosecution may be expedited.

Respectfully submitted,

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